March 31 , 2005

Ms. Gail M. Garvin
Dow AgroSciences LLC
9330 Zionsville Road
Indianapolis, IN 46268

Dear Ms. Garvin:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the test plans and robust summaries for Methyl chloropyridine derivatives (CAS No. 70024-85-0) and Chloropyridine derivatives (CAS No. 68412-40-8) posted on the ChemRTK HPV Challenge Program Web site on March 5 and March 8, 2004, respectively.

EPA reviews test plans and robust summaries to determine whether they provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for preparing test plans and determining the adequacy of data used to prioritize chemicals for further work.

EPA considers both submissions inadequate for the following reasons: (1) no useful information was provided on the chemical identities of the methyl chloropyridine derivatives and chloropyridine derivatives streams (are mono- or dichlorinated derivatives present? can more than one methyl group be present? can methyl groups be chlorinated? In the methyl chloropyridines robust summary, even the barely minimal substance identification is incorrect); (2) no information was provided on proportions or percent ranges of chemical components in these streams; (3) the test plans do not adequately support the use of 2,3,4,5,6-pentachloropyridine (PCP, CAS No. 2176-62-7) data to address all endpoints for methyl chloropyridine derivatives and chloropyridine derivatives streams for the purposes of the HPV Challenge Program. Moreover, without adequate constituent information it is uncertain whether any single chemical could be an acceptable analog for either mixture.

EPA believes that PCP is not an appropriate analog for the methyl chloropyridine derivatives or for the chloropyridine derivatives streams because (1) the percentage of PCP (as a component of the steams) is not provided; (2) the physicochemical and environmental fate properties of PCP may differ significantly from less chlorinated derivatives; (3) PCP's relatively low water solubility and low reactivity suggest that it will be metabolized differently than less chlorinated components that may be more soluble, more reactive or more toxic to mammalian species; (4) PCP may overestimate the acute and chronic aquatic toxicity of less chlorinated pyridines in the streams by as much as two orders of magnitude; and (5) for the methyl chloropyridine derivatives, mammalian and aquatic toxicity may increase or decrease depending on the placement of methyl groups or chlorine atoms (for example, chlorines on methyl groups may increase toxicity relative to ring-substituted chlorines because of increased reactivity as leaving groups). The methyl group also offers an additional point of metabolic attack. Because of expected differences in physicochemical properties and environmental fate endpoints between PCP and less chlorinated derivatives and because toxicity could vary in either direction for components of the sponsored substances compared to PCP, the latter does not appear likely to be representative of the chlorinated pyridine derivatives or methyl chlorinated derivatives.

The closed system intermediate (CSI) claims (referred to in both test plans as "site-limited intermediate")

are inadequate on the basis of the information submitted. Missing are descriptions of all major unit operations from manufacturing through processing, storage and disposal; information on potential releases during operations; worker exposure; monitoring data showing no detection of methyl chloropyridine derivatives or chloropyridine derivatives in any medium; information on transport from the production site (for chloropyridine derivatives); data on the presence or absence of these streams in distributed products; and supporting evidence that these streams are not present in other end products. For a more complete description of the CSI criteria, please refer to "The Guidance for Testing Closed System Intermediates for the Challenge Program" (http://www.epa.gov/chemrtk/guidocs.htm). Unless Dow AgroSciences LLC can support these CSI claims with additional documentation, test data will be needed for the repeated dose and reproductive toxicity endpoints, as well as for the acute, genetic, and developmental toxicity endpoints.

EPA notes that Dow AgroSciences LLC conducted two developmental toxicity studies on PCP in 2003 and 2004 after agreeing to sponsor methyl chloropyridine derivatives and chloropyridine derivatives in the HPV Challenge Program. If the reason for this testing was to satisfy the requirements of the HPV Challenge Program, Dow should have waited until the close of the public comment period before initiating any needed testing, in accordance with Program guidance.

EPA will post this letter on the HPV Challenge Web site within the next few days. We ask that Dow AgroSciences LLC advise the Agency, within 90 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If there are any questions about responding to this request, please contact Mr. Mark Townsend, of the HPV Chemicals Branch, at 202-564-8617. Questions about the HPV Challenge Program should be submitted through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber